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Aging is associated with changes in left atrial (LA) structure and function. The present study aimed at describing the effect of aging on LA properties in a large cohort of subjects without structural heart disease. We divided 386 subjects (mean age 58 years [range 16 to 91]; 188 men [49%]) clinically referred for echocardiography according to age groups. The P-wave dispersion (PWD), reflecting total atrial conduction time, was measured on a 12-lead surface electrocardiogram as the difference between maximum and minimum P-wave duration. The PA-TDI duration reflecting the total atrial conduction time was measured on tissue Doppler imaging (TDI) as the time between onset of P wave on surface electrocardiogram to peak A′-wave velocity. Two-dimensional speckle-tracking echocardiography was used to assess LA reservoir function, reflecting LA compliance. In the overall population, mean PWD, PA-TDI, and LA reservoir strain were 43 ± 12 ms, 129 ± 27 ms, and 36 ± 13%, respectively. Increasing age was independently associated with prolonged PWD ($\beta = 0.161$; $p < 0.001$), PA-TDI ($\beta = 0.476$; $p < 0.001$), and reduced LA reservoir strain ($\beta = -0.259$; <0.001), suggesting age-related fibrotic changes of the LA myocardium. The association between age and LA reservoir strain was modulated by body mass index ($\beta = -0.582$; $p < 0.001$) and LA volume index ($\beta = -0.117$; $p = 0.014$). In conclusion, aging is associated with longer PWD and PA-TDI duration along with a decrease in LA reservoir function. Obesity and larger LA volumes are independently associated with reduced LA compliance. **(Am J Cardiol 2017;120:140−147)**

Aging has been associated with structural changes of the left atrium (LA). Besides LA dilation as a marker of chronic left ventricular (LV) diastolic dysfunction,[1−3] increase in LA myocardial fibrosis has been demonstrated and associated with impaired LA function, increase in LA stiffness, and changes in LA electrophysiological properties.[3−5] These structural and functional LA changes have been associated with increased risk of atrial fibrillation and heart failure.[6] P-wave indexes, such as P-wave duration and P-wave dispersion (PWD), indirectly reflect the total conduction time of the LA.[7] Echocardiographic tissue Doppler imaging (TDI) also permits evaluation of the total atrial conduction time (PA-TDI duration), which reflects the extent of both electrical and structural remodeling of the atria.[8] Additionally, 2-dimensional (2D) speckle-tracking echocardiography enables the assessment of LA reservoir strain, a marker of LA compliance.[9] PWD, PA-TDI, and LA reservoir strain may change with aging because of structural remodeling of the LA. The present study aimed at describing the effect of aging on LA properties in a cohort of subjects without structural heart disease.

Methods

A total of 386 patients who were clinically referred for cardiac evaluation and transthoracic echocardiography at the Leiden University Medical Center (The Netherlands) without structural heart disease were evaluated retrospectively.[10,11] Referral reasons included evaluation of dyspnea, chest pain, screening preceding noncardiac intervention, palpitations, and evaluation of patients with high cardiovascular risk profile. Subjects with previous cardiac intervention, known history of coronary artery disease, pacemaker implantation, documented cardiac arrhythmias, LV wall motion abnormalities at rest, and any grade of valvular stenosis or more than mild valvular regurgitation were excluded. Therefore, only patients with structurally and functionally normal hearts on echocardiography and sinus rhythm on the electrocardiogram (ECG) without conduction abnormalities were included in the present evaluation. Patients were selected to obtain approximately equal proportions of gender-matched groups across 5 predetermined age categories: <45, 45 to 54, 55 to 64, 65 to 74, and >75 years.

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See page 146 for disclosure information.

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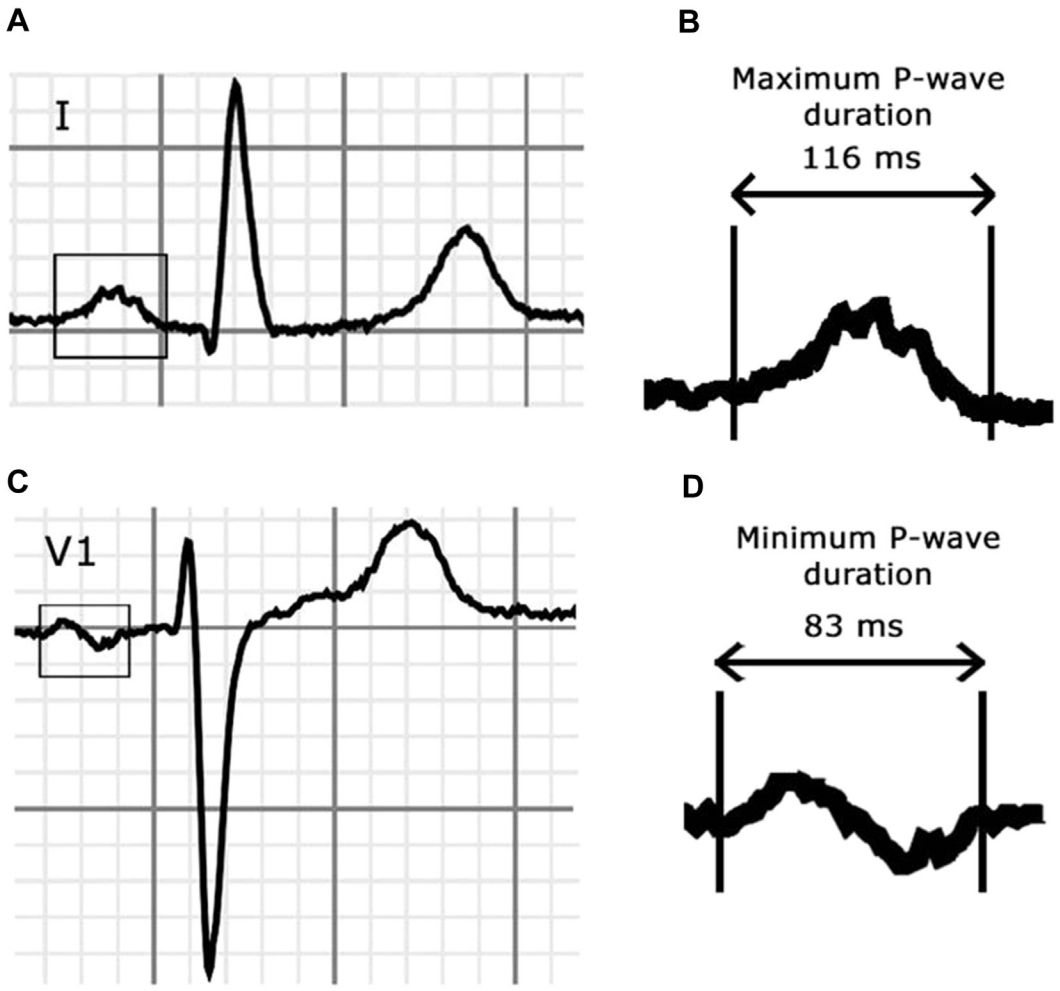

Figure 1. P-wave dispersion measured on 12-lead ECG. *Panel A* shows a full cardiac cycle in lead I obtained from a standard 12-lead ECG. *Panel B* is an enlargement of the box plotted in section A which indicates the maximum P-wave duration. *Panel C* shows 1 full cardiac cycle in lead V1 obtained from a standard 12-lead ECG. *Panel D* shows a zoomed view of the box in section C which indicates the minimal the P-wave duration. The onset and end of the P wave was defined as the point of the first visible upward slope from the isoelectric line and the point of return to isoelectric line. P-wave dispersion is defined as the difference between P-maximum duration and P-minimum duration.

Patient demographics and clinical data were collected. Medications including angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers, β blockers, statins, diuretics, and calcium channel blockers were noted. All clinical data were stored at the departmental Cardiology Information System (EZIS chipsoft and EPD-Vision, Leiden University Medical Center). The Dutch Central Committee on Human-Related Research (CCMO) allows the use of anonymous data without previous approval of an institutional review board provided that the data are acquired for routine patient care. All data used for this study were acquired for clinical purposes and handled anonymously.

The standard 12-lead ECG was recorded at 100 mm/s paper speed and 40 mm/mV calibration. Customized software was used to analyze the PWD (Megacare Infinity VF4; Dräger Medical, Danvers, Massachusetts). PWD was defined as the time difference between maximum P-wave duration and minimum P-wave duration measured in any lead (Figure 1). The onset and end of the P wave were defined as the point of the first visible upward slope from the isoelectric line and the point of return to isoelectric line, respectively. QT interval was corrected for heart rate using the Bazett formula: $QTc = QT/\sqrt{R-R}$.[12]

Echocardiographic data were obtained with patients at rest in the left lateral decubitus position using commercially available ultrasound systems (Vivid 7 and E9; General Electric Vingmed, Horten, Norway). Data acquisition was performed with a 3.5-MHz or M5S transducers. Standard M-mode, 2D, color, pulsed, and continuous-wave Doppler data were acquired and stored digitally for subsequent off-line analysis (EchoPac BT13; GE Medical Systems, Horten, Norway). Left ventricular ejection fraction was calculated using the Simpson's biplane method.[10] LV mass was calculated according to Devereux et al and indexed for body surface area.[10] Diastolic function was measured according to contemporary guidelines.[13] Valvular morphology and function were assessed with 2D, color, pulsed, and continuous-wave Doppler echocardiography.[11] Color-coded TDI data of the LA were obtained from the apical 4-chamber view to measure the PA-TDI duration, an echocardiographic parameter representing the total atrial conduction time (a marker of electromechanical

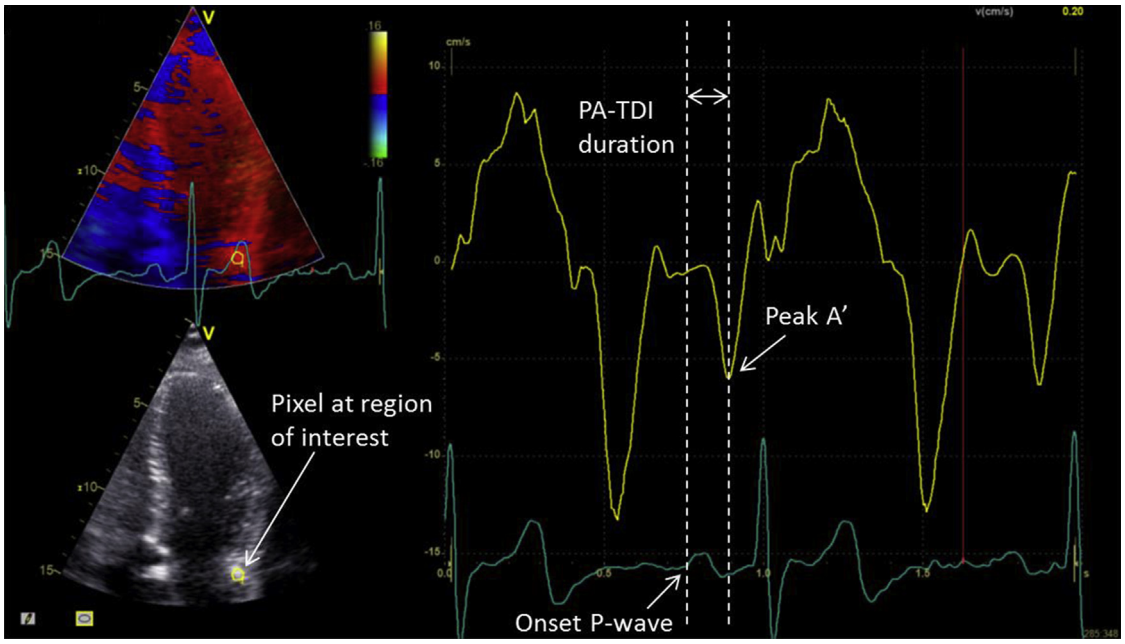

Figure 2. PA-TDI duration by TDI with 2D echocardiography. On bidimensional and TDI image of the apical 4-chamber view, the region of interest is placed in the LA lateral wall above the mitral annulus. This region of interest tracks the movement of the myocardium along the cardiac cycle and the velocity of the myocardium is plotted in the time-velocity curve. The PA-TDI duration is assessed by measuring the time interval between the onset of the P wave in lead II of the surface ECG and the peak A′ wave on the tissue Doppler tracing.

delay—reflecting atrial fibrosis). To assess the PA-TDI duration, a fixed 9 × 9 pixel region of interest was placed on the LA lateral wall just above the mitral annulus to obtain the time velocity tracing of the LA wall. The time interval between the onset of the P wave in lead II of the surface ECG and the peak A′- e on TDI defined the PA-TDI (Figure 2).[8]

LA reservoir strain was evaluated using 2D speckle tracking on the apical 4-chamber view. The ECG was referenced to the onset of the QRS complex or the Q wave, and the region of interest was adjusted to the LA wall thickness. LA reservoir strain was measured as the peak longitudinal strain during ventricular systole (Figure 3).[14]

Continuous variables are reported as mean ± SD. One-way ANOVA was used to compare continuous variables across the groups. Categorical variables are reported as frequencies and percentages and were analyzed using the chi-square test. Pairwise comparisons were performed to assess differences across age categories. Univariate and multivariate linear regression analyses were performed to identify clinical, ECG, and echocardiographic correlates of LA functional characteristics (PWD, PA-TDI, and LA reservoir function). The level of significance for univariate analysis was set at $p < 0.20$. Statistical analysis was performed on SPSS for Windows, v20.0 (IBM, Armonk, New York). A 2-tailed p value < 0.05 was considered statistically significant.

Results

Mean age of the patients was 58 years (range 16 to 91) and 188 (49%) were men. The clinical characteristics of the patients divided according to the 5 pre-determined age categories are presented in Table 1. A total of 365 patients (95%) had analyzable 12-lead surface ECGs (Table 2). The mean PWD was 43 ± 12 ms for the overall population. A significant increase in the duration of PWD across age categories was observed ($p < 0.001$). In contrast, there was no significant difference in the average P wave ($p = 0.100$). Echocardiographic characteristics across the age groups are presented in Table 3. PA-TDI duration analysis was feasible in all patients. The mean PA-TDI duration was 129 ± 27 ms in the overall population. PA-TDI duration significantly increased with aging (Table 3). Analysis of LA reservoir strain was feasible in all patients. The mean LA reservoir strain was 36 ± 13% in the overall population. When analyzing the age categories, LA reservoir strain significantly decreased with aging (Table 3). These findings indicate that aging was associated with slow LA conduction and reduced LA compliance, suggesting the presence of increasing fibrosis of the LA wall.

On multivariate analysis, only age ($\beta = 0.161$; 95% CI 0.074 to 0.248, $p < 0.001$) was independently associated with prolonged PWD (Table 4). In addition, increasing age ($\beta = 0.476$; 95% CI 0.283 to 0.669, $p < 0.001$) was the only independent correlate of prolonged PA-TDI duration (Table 5). Finally, older age ($\beta = -0.259$; 95% CI −0.345 to −0.174, $p < 0.001$), larger body mass index ($\beta = -0.582$; 95% CI −0.883 to −0.280, $p < 0.001$), and larger LA volume index ($\beta = -0.117$; 95% CI −0.331 to −0.022, $p = 0.025$) were independently associated with more impaired LA reservoir strain (Table 6).

Discussion

The present study reports the values of PWD, PA-TDI, and LA reservoir strain across a wide age range in a large group of subjects without structural heart disease. With

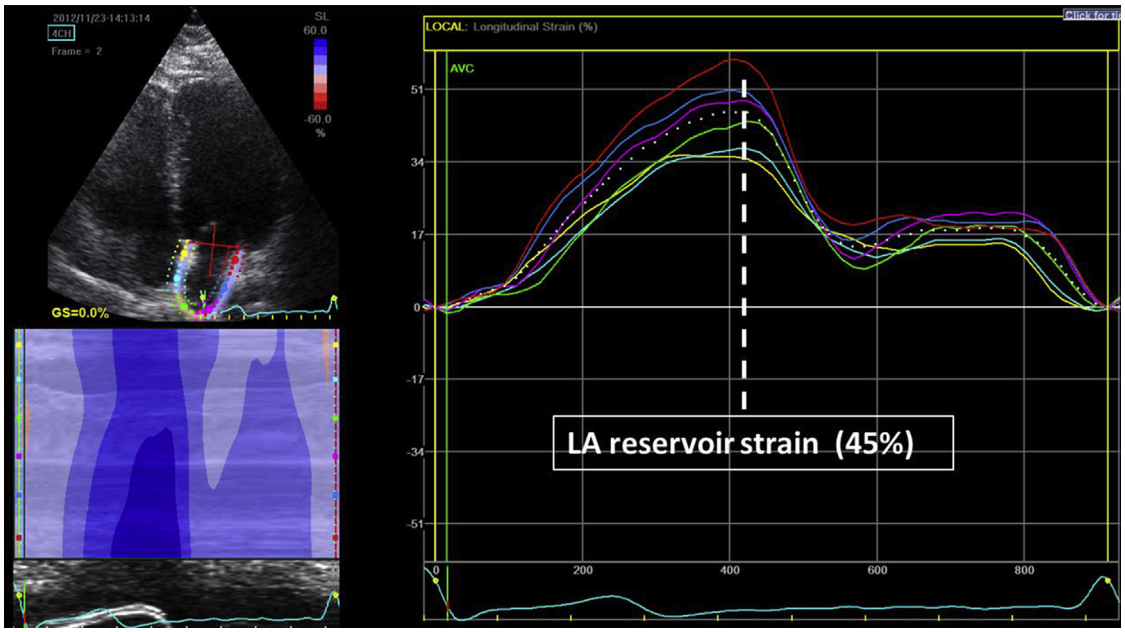

Figure 3. Left atrial speckle tracking with 2D echocardiography. The LA endocardium is manually traced in the apical 4-chamber view, and the region of interest is adjusted to fit the thickness of the LA wall. Strain curves for individual segments are illustrated. LA reservoir strain is measured as the peak global longitudinal strain during ventricular systole, which is indicated by the dotted line within the strain curves.

Table 1
Clinical characteristics divided by age categories

Variable	Age category (years)					
	<45 (n=78)	45-54 (n=79)	55-64 (n=83)	65-74 (n=78)	>75 (n=68)	p-value
Age (years)	34 ± 8	49 ± 3	59 ± 3	69 ± 3	80 ± 4	——
Men	41 (53%)	41 (52%)	40 (48%)	38 (49%)	28 (41%)	0.674
BSA (m^2)	1.9 ± 0.2	1.9 ± 0.2	1.9 ± 0.2	1.9 ± 0.2	1.9 ± 0.2	0.171
BMI (Kg/m^2)	24 ± 3	25 ± 4	26 ± 5	26 ± 4	26 ± 4	0.026
Hypertension	13 (17%)	19 (24%)	27 (33%)	37 (47%)	44 (65%)	<0.001
Hypercholesterolemia	3 (4%)	9 (11%)	17 (21%)	22 (28%)	17 (25%)	0.001
Diabetes Mellitus	2 (3%)	10 (13%)	11 (13%)	14 (18%)	6 (9%)	0.062
(Ex-) Smoker	17 (22%)	22 (28%)	25 (30%)	26 (33%)	16 (24%)	0.029
Family history CVD	30 (39)	32 (41)	27 (33)	17 (22)	16 (24)	0.008
ACEi	5 (6%)	9 (12%)	10 (12%)	18 (22%)	10 (15%)	0.042
ARB	3 (4%)	6 (8%)	9 (11%)	10 (13%)	13 (20%)	0.030
Beta-blocker	6 (8%)	8 (10%)	12 (15%)	19 (24%)	15 (23%)	0.014
Ca channel blocker	5 (6%)	5 (7%)	7 (9%)	8 (10%)	10 (15%)	0.340
Statins	3 (4%)	11 (13%)	20 (24%)	22 (28%)	18 (28%)	<0.001
Diuretics	7 (9%)	9 (12%)	6 (7%)	14 (18%)	23 (35%)	<0.001

Data are presented as mean ± standard deviation or as number (percentage).

Hypertension was defined as blood pressure ≥140/90 mm Hg or using anti-hypertensive therapy. Hypercholesterolemia was defined as total cholesterol 190 mg/dl or using lipid-lowering medication. Diabetes mellitus was defined as fasting blood glucose ≥7.0 mmol/L, 2-h oral glucose tolerance test glucose ≥11.1 mmol/L or using anti-diabetic medication.

ACEi = angiotensin converting enzyme inhibitor; ARB = angiotensin II receptor blocker; BMI = body mass index; BSA = body surface area; Ca = calcium; CVD = cardiovascular disease.

increasing age, the LA conduction becomes slower and the LA compliance reduces, suggesting the presence of age-related fibrotic changes of the LA wall. In addition, larger body mass index and LA volume index were independently associated with reduced LA reservoir strain.

Aging is related to structural remodeling of the LA myocardium.[3–5] This structural remodeling may become pathologic and form the substrate for the occurrence of atrial fibrillation or lead to heart failure.[6,15] Differentiation between physiological and pathologic LA structural remodeling is challenging. Current noninvasive imaging techniques permit evaluation of LA dimensions and geometry and LA myocardial tissue characterization. Dilated LA and the presence of macroscopic fibrosis on magnetic resonance

Table 2
Electrocardiographic characteristics divided by age categories

Variable	Age category (years)					
	<45 (n=73)	45-54 (n=72)	55-64 (n=82)	65-74 (n=75)	>75 (n= 63)	p-value
Heart rate (bpm)	73 ± 16	71 ± 13	68 ± 11	74 ± 14	72 ± 11	0.027
PR interval (ms)	149 ± 20	156 ± 21	160 ± 21	170 ± 25	178 ± 29	<0.001
QRS duration (ms)	96 ± 13	97 ± 13	96 ± 14	96 ± 15	95 ± 16	0.963
QTc interval (ms)	395 ± 24	398 ± 36	409 ± 20	403 ± 22	409 ± 22	0.001
P-wave duration (ms)	92 ± 8	91 ± 8	95 ± 8	94 ± 9	93 ± 9	0.100
P-wave dispersion (ms)	37 ± 12	41 ± 10	41 ± 10	45 ± 12	49 ± 12	<0.001

Data are presented as mean ± standard deviation.
bpm = beats per minute.

Table 3
Echocardiographic characteristics divided by age categories

Variable	Age category (years)					
	<45 (n=78)	45-54 (n=79)	55-64 (n=83)	65-74 (n=78)	>75 (n=68)	p-value
Heart rate (bpm)	72 ± 14	71 ±13	67 ± 11	72 ± 12	71 ± 11	0.485
Ventricular septum (mm)	10 ± 1.7	10 ± 1.5	10 ± 1.5	10 ± 2.1	10 ± 1.7	0.004
LV end-diastolic diameter (mm)	48 ± 5	48 ± 7	48 ± 6	49 ± 7	47 ± 6	0.707
LV end-systolic diameter (mm)	31 ± 6	30 ± 5	31 ± 7	32 ± 7	30 ± 5	0.170
LV posterior wall diameter (mm)	10 ± 3	10 ± 2	10 ± 3	10 ± 2	10 ± 1	0.916
LV mass, indexed (g/m^2)	77 ± 26	78 ± 22	82 ± 23	84 ± 22	87 ± 22	0.089
LV end-diastolic volume (ml)	121 ± 30	108 ± 30	110 ± 29	99 ± 27	90 ± 23	<0.001
LV end-systolic volume (ml)	51 ± 19	43 ± 17	45 ± 17	38 ± 15	34 ± 12	<0.001
LV ejection fraction (%)	62 ± 5	62 ± 7	60 ± 8	62 ± 7	62 ± 7	0.684
LA diameter (mm)	34 ± 4	35 ± 5	35 ± 6	36 ± 5	37 ± 5	0.028
LA indexed volume (ml/m^2)	23 ± 7	22 ± 7	25 ± 7	24 ±9	24 ± 7	0.231
LA reservoir strain (%)	43 ± 14	39 ± 12	35 ± 11	34 ± 11	29 ± 9	<0.001
PA-TDI (ms)	116 ± 23	121 ± 23	131 ± 24	133 ± 23	145 ± 29	<0.001
E/A ratio	1.4 ± 0.4	1.2 ± 0.3	1.1 ± 0.3	0.9 ± 0.3	0.9 ± 0.4	<0.001
E′ (cm/s)	16.3 ± 3.4	13.2 ± 3.3	11.8 ± 2.4	9.7 ± 2.7	8.7 ± 3.0	<0.001
E/E′	4.9 ± 1.2	5.8 ± 2.2	6.2 ± 1.5	8.2 ± 7.8	8.9 ± 4.3	<0.001

Data are presented as mean ± standard deviation.
bpm = beats per minute; LA = left atrial; LV = left ventricular; TDI = tissue Doppler imaging.

Table 4
Univariate and multivariate linear regression analyses to explore correlates of P-wave dispersion

Variable	Univariate analysis			Multivariate analysis		
	β	95% CI	p-value	β	95% CI	p-value
Gender	0.482	-1.917 to 2.881	0.693	——	————	——
BMI (kg/m^2)	0.281	-0.015 to -0.578	0.063	0.091	-0.213 to 0.394	0.558
Age (years)	0.226	0.155 to 0.297	<0.001	0.161	0.074 to 0.248	<0.001
Hypertension	4.362	-1.929 to 6.794	<0.001	2.012	-1.194 to 5.217	0.218
Hypercholesterolemia	1.058	-2.091 to 4.208	0.509	——	————	——
Diabetes mellitus	1.292	-2.475 to 5.058	0.501	——	————	——
ACEi-ARBs	1.825	-0.959 to 4.609	0.198	-1.838	-5.131 to 1.455	0.273
Beta-blocker	4.053	0.773 to 7.334	0.016	1.925	-1.486 to 5.336	0.268
Statins	0.713	-2.349 to 3.776	0.647	——	————	——
LA reservoir strain (%)	-0.151	-0.248 to -0.054	0.002	-0.025	-0.130 to 0.081	0.645
LA volume, indexed (ml/m^2)	0.051	-0.106 to 0.209	0.524	——	————	——
PA-TDI (ms)	0.099	0.054 to 0.143	<0.001	0.046	-0.002 to 0.094	0.058

ACEi = angiotensin converting enzyme inhibitor; ARB = angiotensin II receptor blocker; BMI = body mass index; CI = confidence interval; LA = left atrial; LV = left ventricular; TDI = tissue Doppler imaging.

Table 5
Univariate and multivariate linear regression analyses to evaluate correlates of left atrial conduction time on tissue Doppler imaging (PA-TDI)

Variable	Univariate analysis			Multivariate analysis		
	β	95% CI	p-value	β	95% CI	p-value
Gender	2.846	-2.463 to 8.155	0.292	——	——————	——
BMI (kg/m^2)	0.808	0.157 to 1.458	0.015	0.132	-0.547 to 0.812	0.702
Age (years)	0.637	0.485 to 0.789	<0.001	0.476	0.283 to 0.669	<0.001
Hypertension	11.194	5.758 to 16.630	<0.001	0.455	-6.775 to 7.686	0.902
Hypercholesterolemia	7.308	0.356 to 14.260	0.039	1.003	-9.996 to 12.003	0.858
Diabetes mellitus	8.094	-0.327 to 16.514	0.060	3.133	-5.869 to 12.135	0.494
ACEi-ARBs	10.363	4.200 to 16.527	0.001	3.493	-4.000 to 10.987	0.360
Beta-blocker	5.561	-1.761 to 12.884	0.136	-1.314	-9.102 to 6.473	0.740
Statins	6.514	-0.252 to 13.279	0.059	-1.070	-11.688 to 9.548	0.843
P-wave dispersion (ms)	0.513	0.282 to 0.744	<0.001	0.230	-0.005 to 0.465	0.055
LA volume, indexed (ml/m^2)	0.525	0.177 to 0.874	0.003	0.294	-0.049 to 0.636	0.093
LA reservoir strain (%)	-0.422	-0.630 to -0.214	<0.001	-0.089	-0.326 to 0.147	0.458

ACEi = angiotensin converting enzyme inhibitor; ARB = angiotensin II receptor blocker; BMI = body mass index; CI = confidence interval; LA = left atrial; LV = left ventricular.

Table 6
Univariate and multivariate linear regression analyses to assess correlates of left atrial reservoir function

Variable	Univariate analysis			Multivariate analysis		
	β	95% CI	p-value	β	95% CI	p-value
Gender	0.454	-2.080 to 2.978	0.724	——	——————	——
BMI (kg/m^2)	-0.901	-1.207 to -0.595	<0.001	-0.582	-0.883 to -0.280	<0.001
Age (years)	-0.292	-0.364 to -0.219	<0.001	-0.259	-0.345 to -0.174	<0.001
Hypertension	-2.754	-5.374 to -0.134	0.039	1.890	-0.748 to 4.528	0.160
Hypercholesterolemia	-3.113	-6.407 to 0.182	0.064	-0.494	-3.876 to 2.889	0.744
Diabetes mellitus	-4.437	-8.457 to -0.416	0.031	-1.273	-5.314 to 2767	0.536
ACEi-ARBs	-0.467	-3.445 to 2.510	0.758	——	——————	——
Beta-blockade	-0.652	-4.135 to 2.831	0.713	——	——————	——
Statins	-2.103	-5.321 to 1.115	0.200	——	——————	——
P-wave dispersion (ms)	-0.170	-0.279 to -0.061	0.002	-0.031	-0.138 to 0.075	0.562
LA volume, indexed (ml/m^2)	-0.293	-0.460 to -0.126	0.001	-0.177	-0.331 to -0.022	0.025
PA-TDI (ms)	-0.095	-0.141 to -0.048	<0.001	-0.017	-0.065 to 0.032	0.496

ACEi = angiotensin converting enzyme inhibitor; ARB = angiotensin II receptor blocker; BMI = body mass index; CI = cinfidence interval; LA = left atrial; LV = left ventricular; TDI = tissue Doppler imaging.

imaging are the hallmark of LA structural remodeling.[16] However, dilation of the LA is rather unspecific and not always pathologic (e.g., in endurance athletes) and detection of macroscopic fibrosis with late gadolinium contrast-enhanced magnetic resonance requires high expertise in image acquisition and postprocessing and its availability remains low.

The present study proposed 3 parameters that characterize the LA structural remodeling combining electromechanical properties of the LA wall and evaluated the age-related changes of these parameters and their correlates. The increased collagen deposition and myocardial fibrosis of the LA myocardium associated with aging lead to slow conduction of the action potential which is reflected by prolongation of the PWD on ECG and PA-TDI duration on echocardiography. In addition, this increased myocardial fibrosis may result in reduced LA compliance which is reflected by reduced LA reservoir strain on echocardiography.

There is accumulating evidence concerning the potential role of PWD, PA-TDI, and LA reservoir strain for risk stratification of patients with various cardiovascular pathologies. However, reference values indicating normal LA physiological properties have not been well established. Data from the Framingham Heart Study including 295 patients (age range between 25 and 85 years, 52% men) showed a median PWD of 34 ms (interquartile range 28 to 43 ms).[17] In addition, a recent meta-analysis including 80 studies with a total of 6,827 healthy participants aged between 25 and 45 years reported a weighted mean value of PWD of 33.46 ± 9.65 ms.[18] The present study reports slightly longer PWD values (43 ± 12 ms) than previous studies,[17,18] but this may be related to a larger proportion of subjects aged >75 years (17%) in the present study (13% in the Framingham Heart Study while the meta-analysis included age categories up to 45 years of age).[18]

Several studies have shown the age dependency of PA-TDI duration.[19,20] Erdem et al[19] demonstrated in 80 healthy subjects aged between 20 and 40 years that the PA-TDI duration increased with older age (β = 0.342,

$p = 0.001$). Weijs et al[20] evaluated the correlates of PA-TDI in 427 patients and reported a mean PA-TDI duration of 157 ± 22 ms, whereas age was independently associated with increasing PA-TDI on multivariable analysis (each 10-year increase in age was associated with 5 ms increase in PA-TDI). However, that study included a broad spectrum of patients (with history of atrial fibrillation, heart failure, and valvular heart disease), and therefore, the PA-TDI values do reflect more than just the effect of aging.

Finally, the association between aging and changes in LA reservoir strain has been demonstrated in previous studies.[3,5,21,22] In 188 healthy subjects (21 to 80 years; 43% male) free of cardiovascular disease or cardiovascular risk factors, Boyd et al[21] showed that TDI-derived global longitudinal strain of the LA (representing reservoir function) was independently associated with age. Interestingly, the reduction in LA reservoir strain was apparent from the sixth decade, whereas LA dilation was observed from the seventh decade, suggesting that LA strain measures may be more sensitive of structural LA changes than conventional echocardiographic parameters. In the present study, there were no significant changes in LA volume and LV mass. However, we did observe a higher prevalence of diastolic dysfunction with increasing age. The association between age and LA reservoir strain was modulated by LA volume, suggesting that diastolic dysfunction leads to dilation of the LA, and therefore, the influence of age on LA reservoir strain is reduced. In addition, the present study demonstrated that LA reservoir strain is independently associated with BMI. In overweight and obese patients, it has been demonstrated that the increase of epicardial fat tissue is associated with increased LA dimensions and reduced LA compliance.[23] In 70 patients (including 50% obese patients, with BMI $\geq$30 kg/m^2), Erdem et al[24] showed that LA reservoir strain was significantly more reduced in obese patients compared with their counterparts (33.1 ± 8.8% vs 46.2 ± 8.9%, $p < 0.001$, respectively).

Several limitations should be acknowledged. The present study was retrospective in nature and did not include "healthy" subjects because a significant proportion had cardiovascular risk factors or used cardiovascular medication that may influence LA mechanics. However, after correction for these confounding factors, there were strong associations between age and electromechanical properties of the LA. The clinical implications of these findings remain unknown and future studies are needed to demonstrate whether therapy (control of risk factors) may modulate the age-related changes in the electromechanical properties of the LA. Furthermore, a longitudinal design of the study would have allowed for evaluation of changes in LA electromechanical properties according to changes in loading conditions. In addition, late gadolinium contrast-enhanced cardiac magnetic resonance was not performed to demonstrate the presence of LA fibrosis and correlate it with the electromechanical LA properties. Finally, LA strain measurements were performed with dedicated post-processing software, and the values obtained with this software may not be generalized to other vendors.

Disclosures

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